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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 04/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,527	BARANY ET AL.	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *1-14 and 25-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/9/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group III, claims 15-24 in Paper No. 11122003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Applicant's election with traverse of Group III, claims 15-24 and the species election of : 1) oligonucleotide probe sequence of SEQ ID NO: 2; 2) a probe sequence length of 24 mers; 3) the oligonucleotide analog probe sequence of SEQ ID NO: 2 where 5-propynyl-uracil is utilized; 4) the oligonucleotide target which is the complement of SEQ ID NO: 2; 5)and 6) solid substrate made from polyacrylamide; 7) propynyl dU phosphromidite as the reagent, in Paper No. 11122003 is acknowledged. The traversal is on the ground(s) that the groups of invention and species identified are closely related and therefore would require common areas of search and consideration. Applicants arguments regarding the closely related groups of inventions has been considered and is not persuasive, since the different groups of inventions have different properties or method steps and which have uses of the products, e.g., group IV inventions are drawn to a different methods of using oligonucleotide arrays compared to the elected group III method. The method steps of groups III and IV are different and thus the inventions are distinct from each other. And further applicants arguments regarding the request for declaration of interference under 37 CFR 1.607(a) and the copied claims are substantially same as the issued patent 6,156,501, have been considered and are not persuasive because a) it is irrelevant whether the claims were examined in a different application together, and the instant application is

different from the issued patent, and b) the interference as proposed by applicants has not decided. Thus the restriction requirement is proper. The species election requirement has been made to aid in searching and examining the application, and the claims are not limited to the elected species.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-14, 25-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11122003.

Priority

4. This application is a CIP of 08/794,851 filed on 2/4/097, which claims benefit of 60/011,359, filed on 2/9/1996.

Specification

5. The disclosure is objected to because of the following informalities: the last line of pages 48, 49, 52 is not clearly visible.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

7. Claims 15-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites 'oligonucleotide analogue array', it is not clear what does applicants mean by analogue array. Does applicants mean that the array has sequences, which are analogous to the target sequences, or does applicants mean that the analogue array has oligonucleotide analogies used in the probe synthesis. The metes and bounds of the 'analogue array' are not clear. Applicants are requested to amend the claim to clarify the issue. The specification teaches the use of peptide nucleotide analogues in the array synthesis, if applicants mean that the instant claim array is prepared using PNAs. Applicants are requested to amend the claim.

Claim 15 recites the limitation "said oligonucleotide analogue probe array" in step b, line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites the limitation "said target nucleic acids" in step c, line 2. There is insufficient antecedent basis for this limitation in the claim.

Claim 15 recites 'similar hybridization stability across the array' it is not clear what does applicants mean by similar stability. The metes and bounds of term similar stability are not clear. Applicants are requested to clarify.

Claim 16 recites the limitation "the thermal stability". There is insufficient antecedent basis for this limitation in the claim or in claim 15.

Claim 16 is vague and indefinite by reciting that 'at least one of said oligonucleotide probes has increased thermal stability... compared to an oligonucleotide probe that is perfect complement to the complementary oligonucleotide..'. It is not clear whether applicants mean that the oligonucleotide probe applicants referring to, which is perfect complement to the complementary oligonucleotide target. Does applicants mean that the analogue probe has a

different oligonucleotide sequence such that the probe has increased stability compared to the probe which is perfect complement to the complementary target.

Claim 16 recites that at least one of said oligonucleotide probes has increased thermal stability. Claim 16 is dependent on claim 15 which recites the array has similar hybridization stability across the array. Thus claim 16 recitation of at least one probe having increased stability contradicts the independent claim 15 recitation. Applicants are requested to amend the claims.

Claim 18 recites the limitation "said target nucleic acid". There is insufficient antecedent basis for this limitation in the claim or in claim 15.

Claim 18 recites the limitation "said hybridization step" in line 2. There is insufficient antecedent basis for this limitation in the claim or in claim 15.

Claim 16 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the use of phosphromidite derivative of 5-propynyl-dU in place of thymine to increase the Tm. The use of phosphromidite derivative of 5-propynyl-dU is essential for increased stability, however the instant claim does not recite the presence of the phosphromidite derivative of 5-propynyl-dU. Applicants are requested to amend the claim.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 15, 19-23 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,412,087 (McGall et al) (US Patent application 07/874,849 filed on 4/24/92).

The instant claim briefly recites a method of analyzing interactions between an oligonucleotide target and an oligonucleotide analogue probe comprising: a)synthesizing an oligonucleotide analogue array; b) exposing said oligonucleotide analogue probe array to oligonucleotide target; c) determining whether an oligonucleotide analogue probe of the array binds to at least one target nucleic acid.

McGall et al teach spatially addressable arrays of oligonucleotides on a solid substrate (refers to the instant claim array). The reference teaches that the arrays can be used in assays to detect the presence of complementary nucleic acid in sample (e.g., see the abstract). The reference teaches that spatially addressed irradiation of predefined regions on the surface permits immobilization of oligonucleotides and other polymers at the activated regions of the surface. The reference teaches that nucleic acids such as RNA and DNA are the polymers and also synthetic, non-naturally occurring monomers can be used to construct a biological polymer (e.g., see column 4) (refers to the oligonucleotide analogies of the instant claims). The reference teaches that the monomers are immobilized to the solid substrate in the predefined regions by selectively irradiating predefined regions to activate photoactivatable thiol groups (e.g., see

column 5)(refers to instant claims 19 and 23). The reference teaches that the substrate can be glass slides (e.g., see column 6) (refers to instant claims 21-22). The reference teaches that array of anti-ligands permits simultaneous screening of liquid sample for ligands having high affinities for certain anti-ligands of the matrix. The reference teaches that the oligonucleotide solution was applied to the slide (refers to instant claim 20). The reference teaches that the arrays were tested for ability to hybridize specifically with a complementary oligonucleotide or target nucleic acid. Thus, the reference clearly anticipates the claimed invention.

10. Claims 15, 22, 24 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 5,723,320 (Dehlinger) (US Patent application 08/520,730 filed on 8/29/95).

Dehlinger et al teach positionally addressable polynucleotide arrays. The reference teaches that the method employs an array of different sequence oligonucleotides having a unique, known combinatorial sequence associated with each addressable region in the array ((e.g., see column 2) (refers to instant claim array). The reference teaches that the array is contacted with gene-probe templates (e.g., see column 2)(refers to the instant claim plurality of oligonucleotide targets). The reference teaches that the contacting is done under complementary strand hybridization conditions (e.g., see column 2). The reference teaches that the oligonucleotides may include nucleotide analog subunits (refers to instant claim oligonucleotide analog). The reference teaches that eh position0addresable array of different oligonucleotides are formed on a wound or extended filament (e.g., see column 3) (refers to instant claim solid substrate). The reference teaches that the suitable polymers for the coating are polystyrene (e.g., see column 7) (refers to instant claim 22). The reference teaches that the use of 3'

phosphromidate activated nucleoside (e.g., see column 8) (refers to instant claim 24). The reference teaches that the probe array of the invention is used in sequencing and in diagnostics. The gene probe array of the invention is contacted with labeled DNA sample (refers to the target oligonucleotide sequence of the instant claims) (refers to step b) of the instant claims) (e.g., see column 13). The reference teaches that the sample binding to the array has been identified (refers to instant claim step c). the reference clearly anticipates the claimed invention.

11. Claims 15-24 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,156,501 (McGall et al) (US Patent application 08/520,730 filed on 8/29/95).

Claims 15-24 are copied from US Patent 6,156,501 (McGall et al) (US Patent application 08/630,427, filed on 4/3/96).

Claims 35, 37, 43-44, 46-48, and 50 of the '501 patent are exactly same as the instant claims 15-24. The '501 patent or the 08/630,427 application is a CIP of 08/440,742, filed on 5/10/95. The 08/440,742 application discloses the oligonucleotide analogues in the synthesis of array. Thus, the '501 patent claims have effective filing date of at least 5/10/1995. The effective filing date of current application 09/986,527 is 2/9/96. Thus the reference the '501 patent clearly is a prior art under 35 USC. 102 (e).

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 15, 17-18, 20-22, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 5,700,637 (Southern) and US patent 5,594,121 (Froehler et al).

The instant claim briefly recites a method of analyzing interactions between an oligonucleotide target and an oligonucleotide analogue probe comprising: a)synthesizing an oligonucleotide analogue array; b) exposing said oligonucleotide analogue probe array to oligonucleotide target; c) determining whether an oligonucleotide analogue probe of the array binds to at least one target nucleic acid.

Southern teaches methods for analyzing a polyucleotide sequence. The reference teaches an array of oligonucleotides on a glass plate (refers to the instant claim array and claims 21-22) (e.g., see abstract). The array of the reference on a glass plate is use din a hybridization reaction. The reference teaches that the polynucleotide sequences of the array of chosen length, the different oligonucleotides occupying separate cells of the array (e.g., see column 1)(refers to the known locations of the instant claim). The reference teaches the use of monomers comprising

phosphromidite nucleotides (e.g., see column 9). The reference teaches that in the hybridization reaction the array is explored with labeled probe, and the probe may comprise labeled sequences amplified from the genomic DNA by polymerase chain reaction (e.g., see column 2) (refers to instant claims 17-18).

The claimed invention differs from the prior art teachings by reciting oligonucleotide analogue array. Southern teaches the method for synthesis of oligonucleotide array and use of the array in a method of detecting the target sequences. Southern does not teach the oligonucleotide analog array. Froehler et al teach modified purine-based oligomers (nucleotide analogues), which have enhanced ability to form duplexes as compared to the use of conventional bases (e.g., see abstract). The reference teaches that the enhanced binding affinity of the reference oligomers is an advantage for their use as probes and primers (e.g., see column 32). The reference teaches that the oligomers having enhanced affinity for complementary nucleic acid sequences or enhanced nuclease stability would have improved properties for diagnostic applications (e.g., see column 3). The reference teaches that the oligomers of the invention can be formed using standard solid phase oligomer synthesis (e.g., see column 11). The reference teaches the use of protecting groups during synthesis, and the use of phosphoramidite as coupling groups (e.g., see column 12) (refers to instant claim 24).

It would have been obvious to one skilled in the art at the time the invention was made to use the oligonucleotide analogs taught by Froehler et al in the array of oligonucleotide taught by Southern because Froehler et al teaches that the oligomers having enhanced affinity for complementary nucleic acid sequences or enhanced nuclease stability would have improved properties for diagnostic applications. A person skilled in the art would have been motivated to

use the modified oligomers taught by Froehler et al with the oligonucleotide array of Southern and use the array in the diagnostic assays because Froehler et al teaches the advantages of the oligomers in the diagnostic assays.

Response to Affidavits

15. The affidavits filed on 1/28/02 under 37 CFR 1.608 (b) have been noted. The Examiner has not yet found the application in condition for declaration of interference, and when the application is in condition for declaration of interference, the examiner will consider the evidence and explanation only to the extent of determining whether a basis upon which the application would be entitled to the judgment relative to the patentee is alleged and if a basis is alleged, an interference may be declared (see MPEP Patent rules 1.609 (b)).

Conclusion

16. No claims are in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner is on Increased Flex Schedule and can normally be reached from Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
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Pp
21 April 2004

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